



Our STN: BL 103234/5033

Amgen, Incorporated  
Attention: Douglas Hunt  
Director, Regulatory Affairs  
One Amgen Center Drive  
Thousand Oaks, CA 91320-1799

**MAY 21 2004**

Dear Mr. Hunt:

Your request to supplement your biologics license application for Epoetin alfa to update the Clinical Experience, Cancer Patients on Chemotherapy subsection of the package insert, has been approved. In addition, the revisions to the Warnings section, and the revisions to the Precautions section of the package insert to include information regarding the observed effects of Epoetin alfa and other products in this class on response rate, time-to-progression and survival in patients with non-myeloid tumors, have been approved.

This fulfills your commitment to conduct and submit the results of a Phase 4 study (Protocol N93-004) to evaluate the possible stimulatory effects of Epoetin alfa treatment on solid tumor growth as stated in commitment number one of the April 1, 1993, approval letter for STN 103234/1015.

We acknowledge your written commitments to conduct a postmarketing study and to disseminate a Dear Health Care Professional Letter as described in your letter of May 18, 2004, as outlined below:

**Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.**

1. To submit a draft "Dear Health Care Professional (Important Prescribing Information)" letter, draft envelope, and list of intended recipients by June 4, 2004, and reach agreement regarding the content of the letter with the Agency by June 18, 2004. Amgen will begin to disseminate the letter and the approved package insert to the oncology and hematology medical communities by July 2, 2004.
2. To conduct a study to establish the impact of Epogen/Procrit administration on overall survival, time-to-progression, and objective tumor response rates in the proposed study entitled, "A Double-Blind, Placebo-Controlled, Randomized Phase 4 Study of Epoetin alfa Versus Placebo in Subjects Receiving First Line Chemotherapy for Metastatic Breast Cancer". The draft protocol will be submitted to the FDA by August 31, 2004, and the final protocol will be submitted to the FDA by December 31, 2004.

Patient accrual will be completed by August 31, 2006, the study will be completed by December 31, 2007, and the final study report will be submitted to the FDA by June 30, 2008.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103234. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 103234. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted), and
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (<http://www.fda.gov/cder/pmc/default.htm>). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see <http://www.fda.gov/cber/gdlns/post040401.htm>) for further information.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels).

The regulatory responsibility for review and continuing oversight for this product transferred from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research effective June 30, 2003. For further information about the transfer, please see <http://www.fda.gov/cder/biologics/default.htm>. Until further notice, however, all correspondence, except as provided elsewhere in this letter, should continue to be addressed to:

CBER Document Control Center  
Attn: Office of Therapeutics Research and Review  
Suite 200N (HFM-99)  
1401 Rockville Pike  
Rockville, Maryland 20852-1448

This information will be included in your biologics license application file.

Sincerely,

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Patricia Keegan, M.D.  
Director  
Division of Therapeutic Biological Oncology Products  
Office of Drug Evaluation VI  
Office of New Drugs  
Center for Drug Evaluation and Research

**CONCURRENCE PAGE**

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